Oral and Craniofacial Reconstruction Using Mesenchymal Stem Cells

Grant Award Details

Oral and Craniofacial Reconstruction Using Mesenchymal Stem Cells

Grant Type: New Faculty I

Grant Number: RN1-00572

Project Objective: The objective of this grant proposal is to characterize orofacial mesenchymal stem cells and determine the feasibility of reconstructing the orofacial defects caused by a variety of diseases such as osteonecrosis of the jaw using mesenchymal stem cells. The study focuses on mesenchymal stem cell characterization, disease model generation, and mesenchymal stem cell-based tissue regeneration in small and large animal models.

Investigator:

Name:	Songtao Shi
Institution:	University of Southern California
Type:	PI

Disease Focus: Bone or Cartilage Disease

Human Stem Cell Use: Adult Stem Cell

Award Value: $3,242,651

Status: Closed

Progress Reports

Reporting Period: Year 2

View Report

Reporting Period: Year 3

View Report

Reporting Period: Year 4

View Report

Reporting Period: Year 5

View Report

Reporting Period: NCE

View Report

Grant Application Details

Application Title: Oral and Craniofacial Reconstruction Using Mesenchymal Stem Cells

Public Abstract: The overall goal of this proposal is to explore a new stem cell-based treatment for major defects in the orofacial regions resulted from burns, physical injuries, genetic diseases, cancers, infectious diseases, and recently, bisphosphonate-associated osteonecrosis of the jaw (BONJ), using the patient's own stem cells obtained from the oral cavity known as orofacial mesenchymal stem cells (OMSCs).

The standard surgical reconstruction of orofacial defects relies on different sources of bone grafts harvested from distant anatomical site of the same patient or other donors. However, those approaches are associated with higher morbidity and unpredictable clinical outcomes. Evidences have shown that bone marrow mesenchymal stem cells (BMMSCs) could be a promising alternative for bone reconstruction but not in the orofacial region. These clinical results may be due, in part, to the fact that orofacial and long bones are derived from different cell origins, termed as neural crest cells and mesoderm, respectively. In addition, OMSCs are readily accessible from the oral cavity and can be easily expanded for cell-based therapies due to their inherently high proliferative capability. These evidences suggest that neural crest cell-associated OMSCs might be a superior cell source for orofacial bone regeneration as compared to BMMSCs.

In this study we will compare human OMSCs and BMMSCs in terms of stem cell characteristics and will test their tissue regeneration capacities in the restoration of orofacial defects including the recently drug-induced bone necrosis defects caused by the commonly used drug, bisphosphonate in our established animal models. Our laboratories have recently demonstrated feasibility of using BMMSCs to partially repair craniofacial defects in mouse models. In this proposed study, we will use OMSCs as a model system to determine whether and how individual OMSCs can be utilized as a novel cell therapy for orofacial tissue regeneration. We anticipate that the patient's own OMSCs will be capable of forming orofacial tissues and will highlight future clinical treatments for orofacial defects.

Statement of Benefit to California:	There is a great clinical demand for developing more optimized approaches to repair facial defects caused by burns, trauma, genetic anomalies, cancers, and recently, the devastating drug-induced osteonecrosis of the jaw associated with the commonly used drug, bisphosphonate (BONJ). Current therapeutic approaches are deficient in supplying appropriate tissues for major facial reconstruction. By generating an optimal supply of human orofacial mesenchymal stem cells (OMSCs) for stem cell-based therapy, we hope to circumvent the limited tissue resource and provide a more superior cell source for future facial tissue regeneration. More importantly, Californians who are head and neck cancer survivors, or suffer esthetic and functionally debilitating orofacial defects will benefit from the advances in stem cell biology and its clinical applications, specifically in the field of orofacial reconstruction. In this proposal, we will expand current knowledge of stem cell biology of OMSC and test the feasibility of utilizing these autologous stem cells in the treatment of diseases such as BONJ. The novel approach in the reconstruction of the orofacial defects using OMSC-based therapy will replace standard paradigm of treatment which involves multiple surgeries, lengthy operating time, cost, and morbidity to the patients. The success of this proposal will not only benefit the people of California, but will have high impact on the state economy by reducing the medical cost and overall financial burden on the State of California Health Insurance.

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